Stage III CRC :
I do 3 months (of CAPOX)

Tanios Bekaii-Saab, MD , FACP
Professor , Mayo Clinic College of Medicine and Science
Program Co-Leader , GI Cancer , Mayo Clinic Cancer Center
Senior Associate Consultant, Mayo Clinic AZ

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NCI Comprehensive Cancer Center
A Cancer Center Designated by the National Cancer Institute

NCCN National Comprehensive Cancer Network®

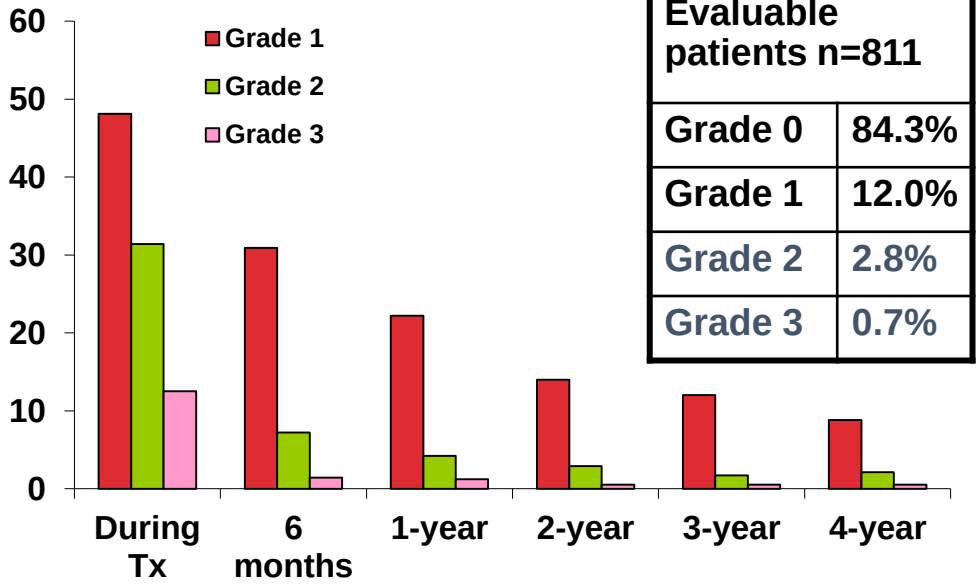
Background and Rationale

- **Previous standard of care for stage III colon cancer patients:**
  6 months of oxaliplatin-based adjuvant therapy with FOLFOX or CAPOX (XELOX)

- **Oxaliplatin is associated with cumulative dose-dependent neurotoxicity**
  - Debilitating for many patients, both short- and long-term
    - Nerve damage (e.g. numbness, tingling, pain) can persist long after discontinuation of therapy, sometimes permanently
  - Dose reductions and early discontinuation of therapy are common

Long-term Safety

Peripheral Sensory Neuropathy



Evaluable patients n=811	
Grade 0	84.3%
Grade 1	12.0%
Grade 2	2.8%
Grade 3	0.7%

Andre et al., JCO 2009

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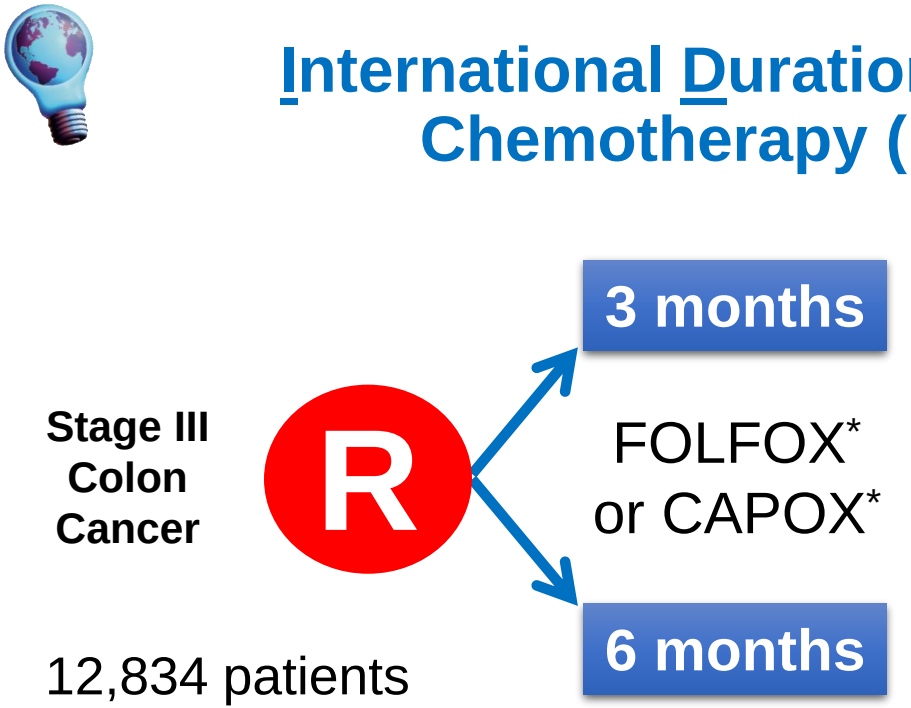
  - Dose reductions and early discontinuation of therapy are common
- **Shorter duration treatment without loss of efficacy would be of benefit to patients and health care resources**

International Duration Evaluation of Adjuvant Chemotherapy (IDEA) Collaboration



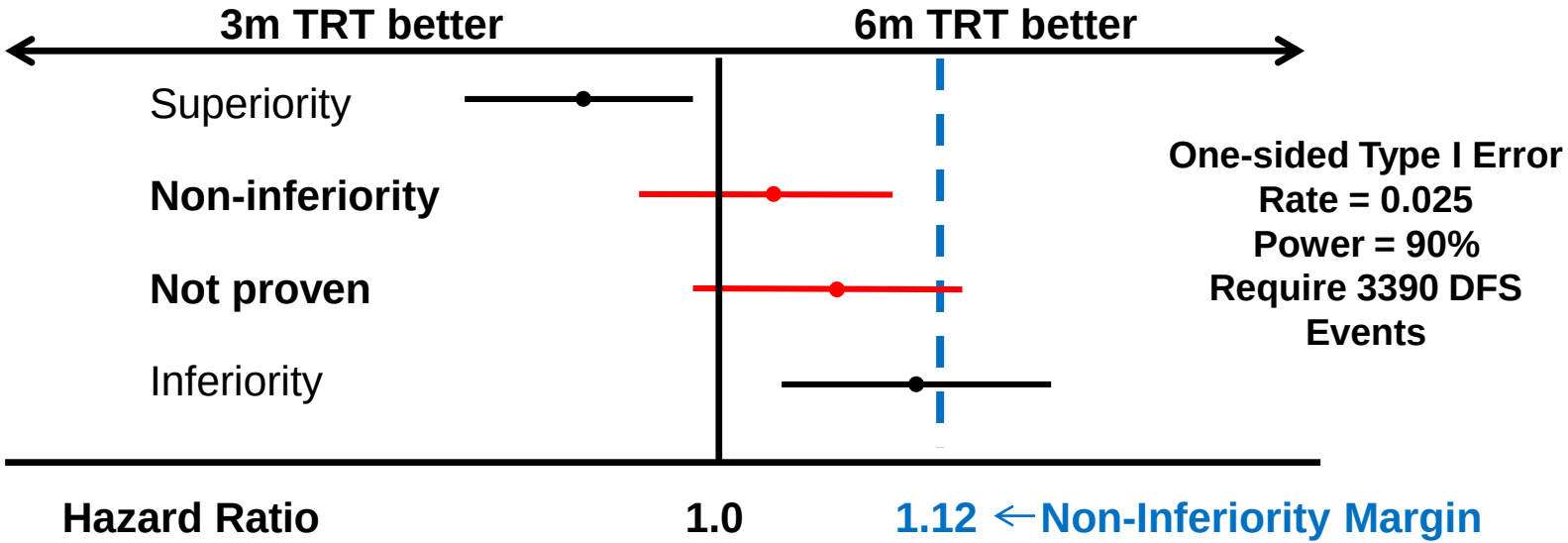
12,834 patients

*Investigator's choice, no randomization

- **Objective:**
  Reduce side-effects of therapy without giving up (too much) anti-cancer efficacy of therapy
- **Non-inferiority design:**
  As agreed upon by patient advocates and oncologists, shorter duration of therapy should not sacrifice more than 12% of benefit of adjuvant therapy
  In statistical terms: upper 95% confidence interval of Hazard Ratio (HR) of disease free survival (DFS) should not exceed *1.12*

Non-Inferiority Hypothesis Testing

Statistical Conclusions Under Different Scenarios

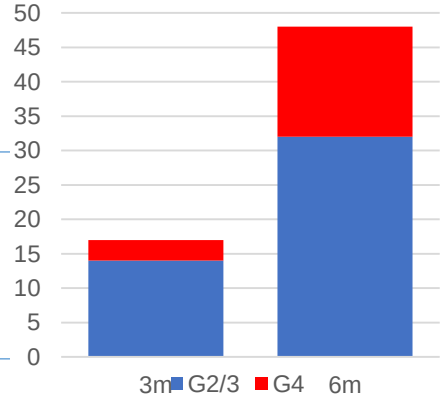


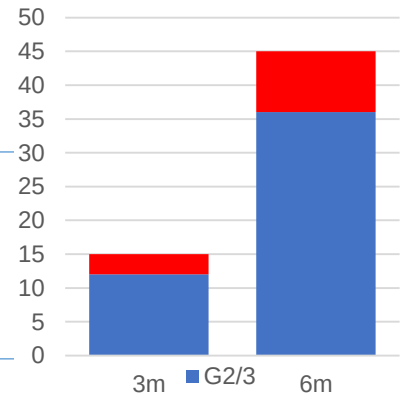
Piaggio et al. JAMA 2012;308(24):2594-2604

TRT: treatment

Adverse Events IDEA trial

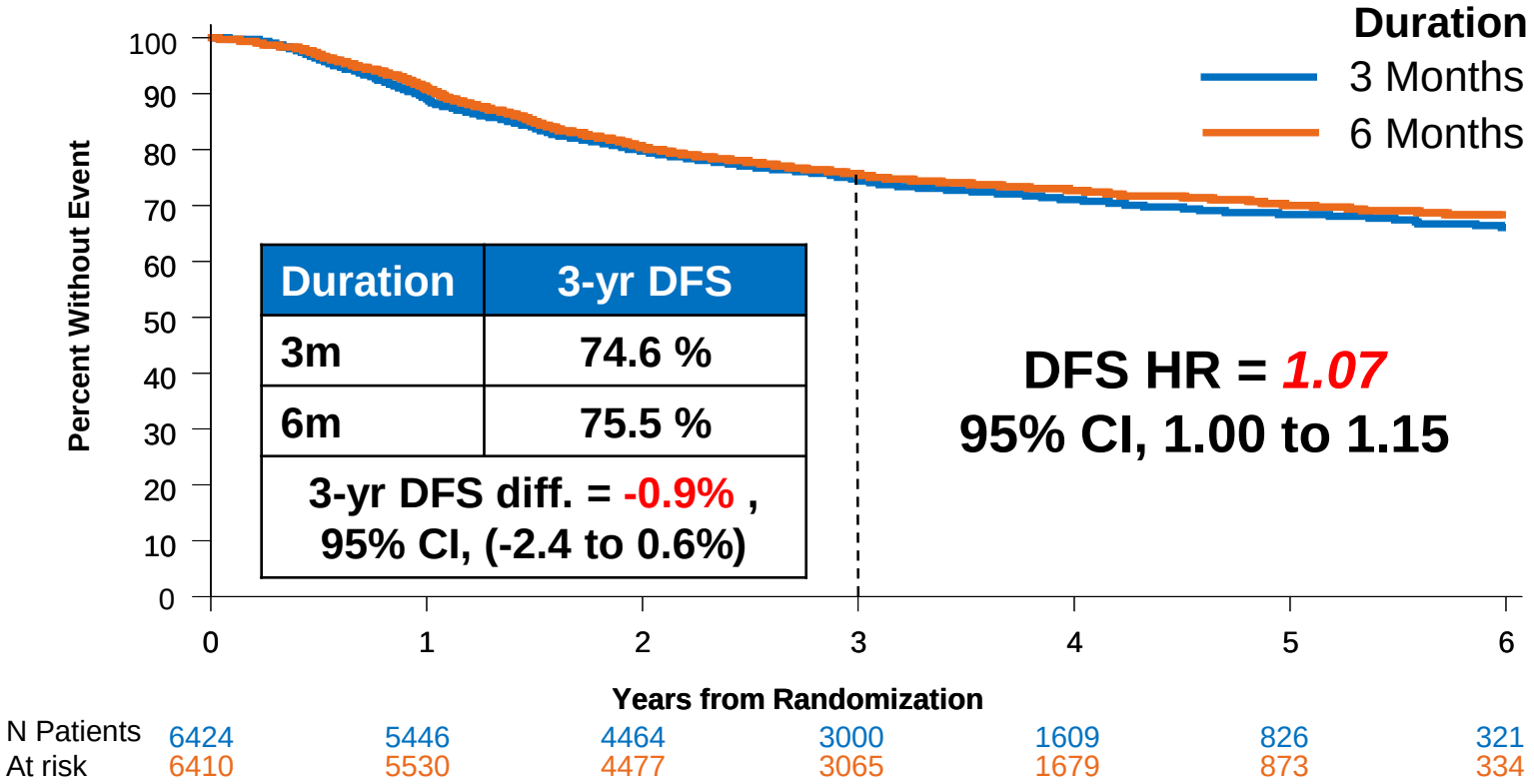
	FOLFOX			CAPOX		
Adverse Events	3m Arm	6m Arm	p-value[1]	3m Arm	6m Arm	p-value[1]
Overall						
G2			<.0001			<.0001
G3-4						
Neurotoxicity						
G2			<.0001			<.0001
G3-4						
Diarrhea						
G2	11%	13%	<.0001	10%	13%	0.0117
G3-4	5%	7%		7%	9%	



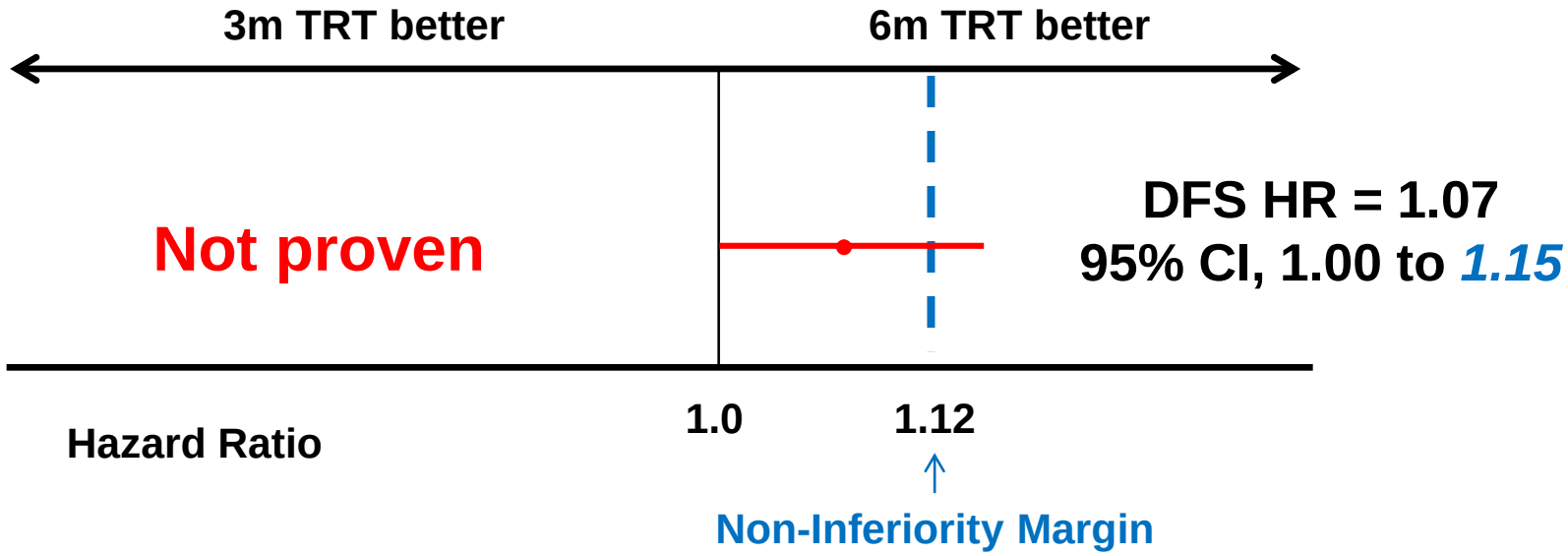


[1]Chi-squared test for trend; Total of 19 grade 5 events; Adverse events only collected on first 617 patients enrolled to SCOT trial

Primary Outcomes Analysis: IDEA trial



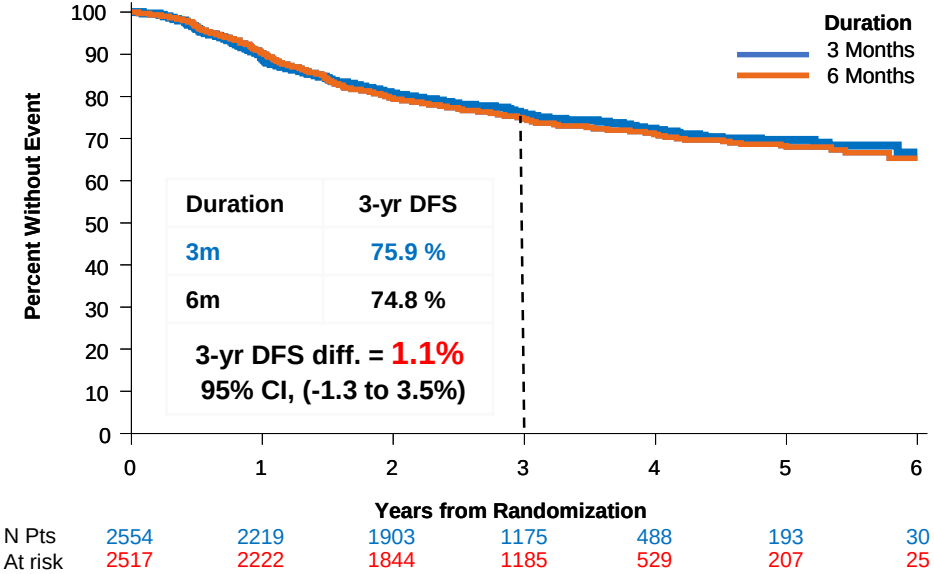
Primary DFS Analysis (mITT), cont.

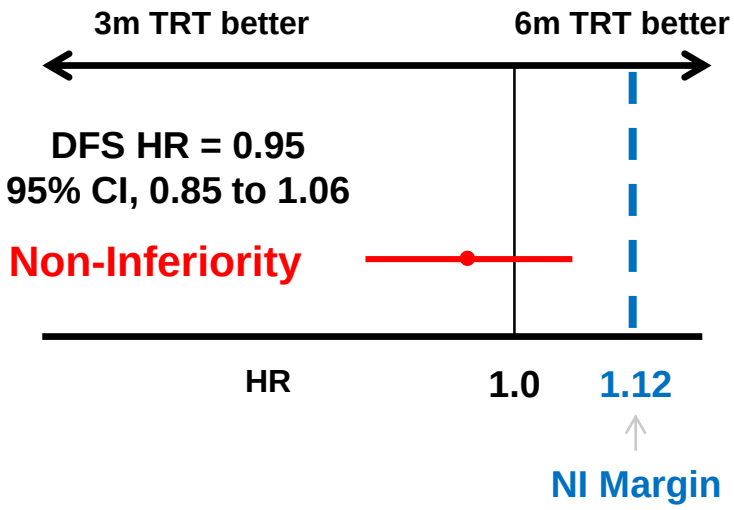


TRT: treatment

3 yr DFS in trial of 3 v 6 months CAPOX in 5071 stage 3 CRC patients proves non inferiority for 3 month regimen!

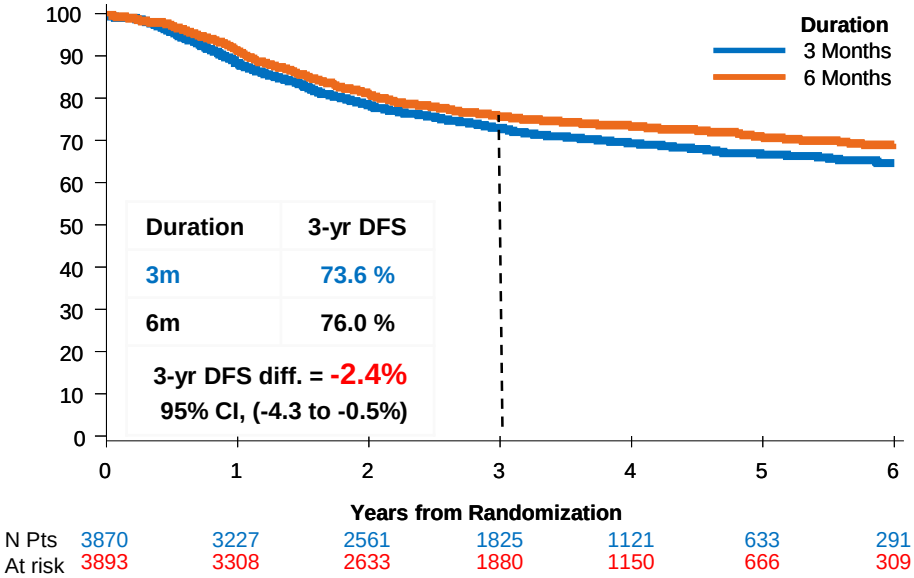
CAPOX

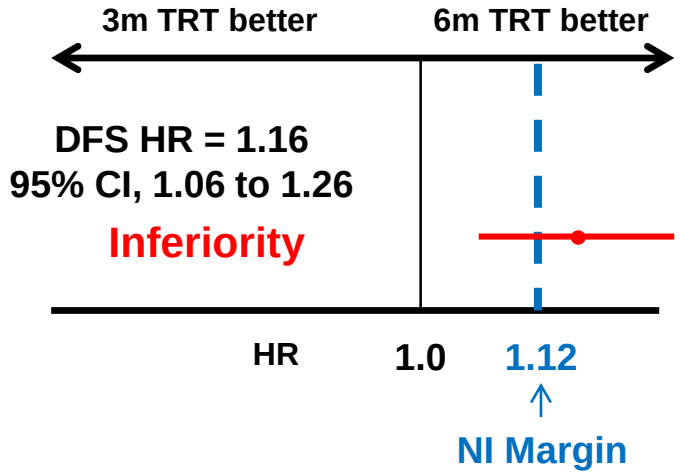




3 yr DFS in trial of 3 v 6 months FOLFOX in 7763 stage 3 CRC patients shows inferiority of 3 month regimen!

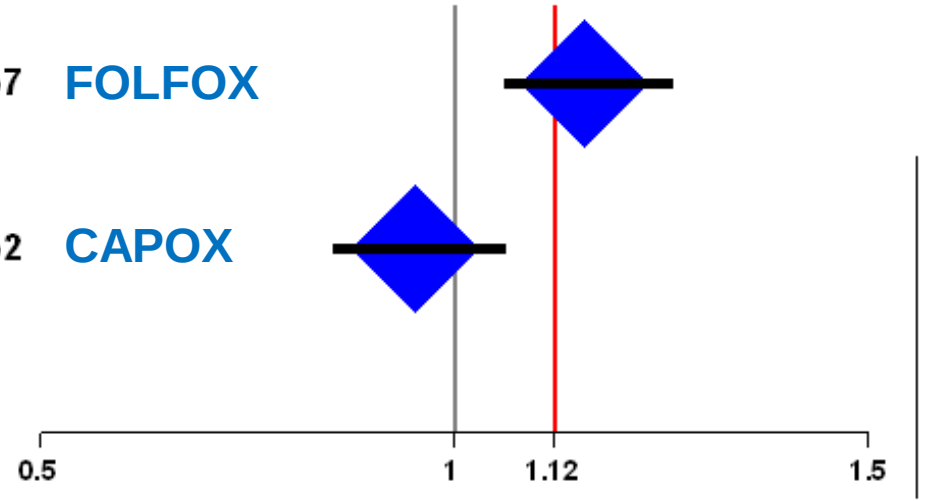
FOLFOX





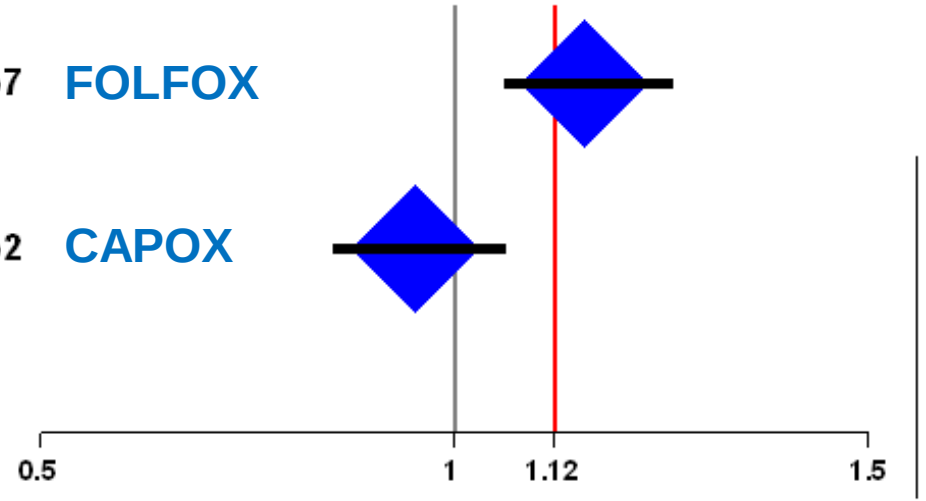
N2 and T4 within high risk stage III: 3 mo vs 6 mo by regimen

N2	441/1072	379/1049	1.159	FOLFOX
N2	275/726	283/720	0.954	CAPOX
Overall	1046/3870	918/3893	1.157	FOLFOX
Overall	637/2554	662/2517	0.952	CAPOX

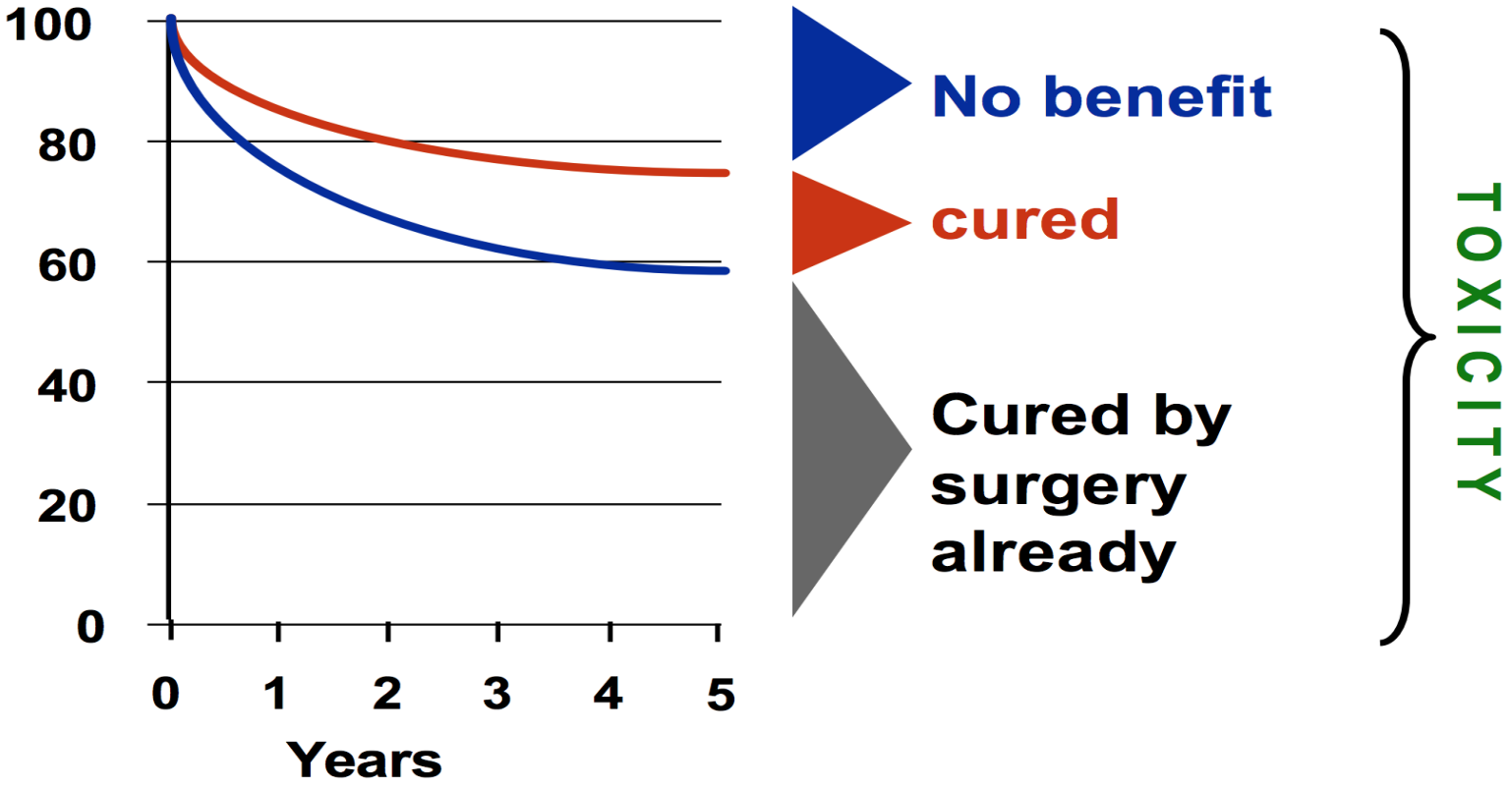


N2 and T4 within high risk stage III: 3 mo vs 6 mo by regimen

N2	441/1072	379/1049	1.159	FOLFOX
N2	275/726	283/720	0.954	CAPOX
T4	302/709	265/718	1.221	FOLFOX
T4	260/611	248/617	1.100	CAPOX
Overall	1046/3870	918/3893	1.157	FOLFOX
Overall	637/2554	662/2517	0.952	CAPOX



Adjuvant Chemotherapy in Stage III CRC



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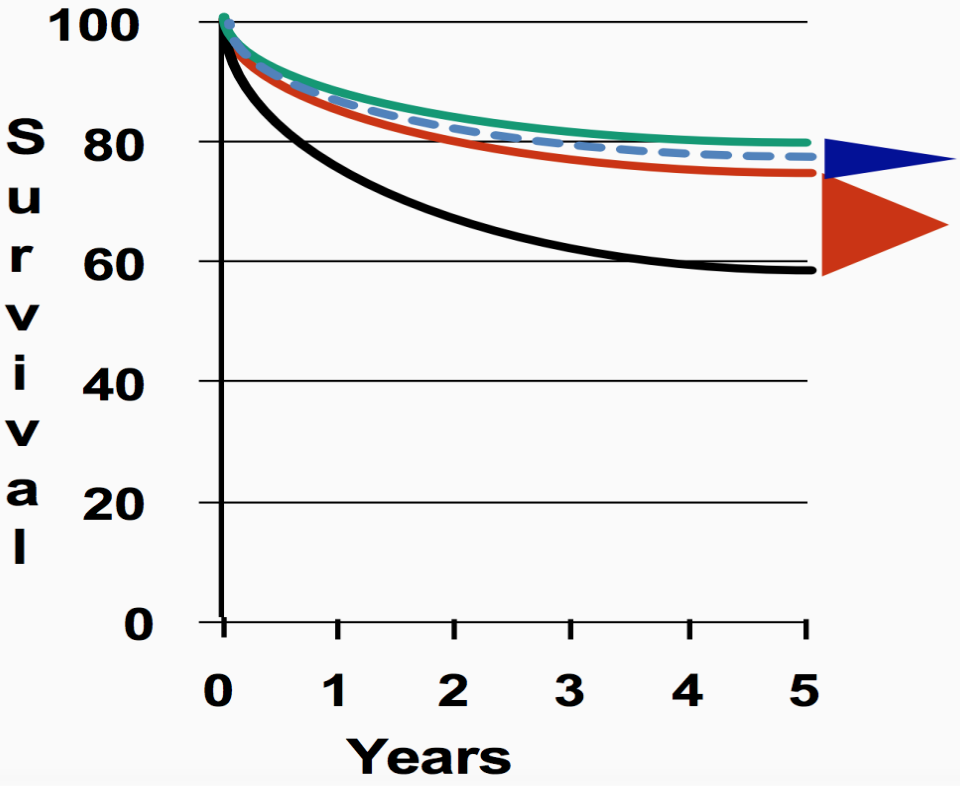


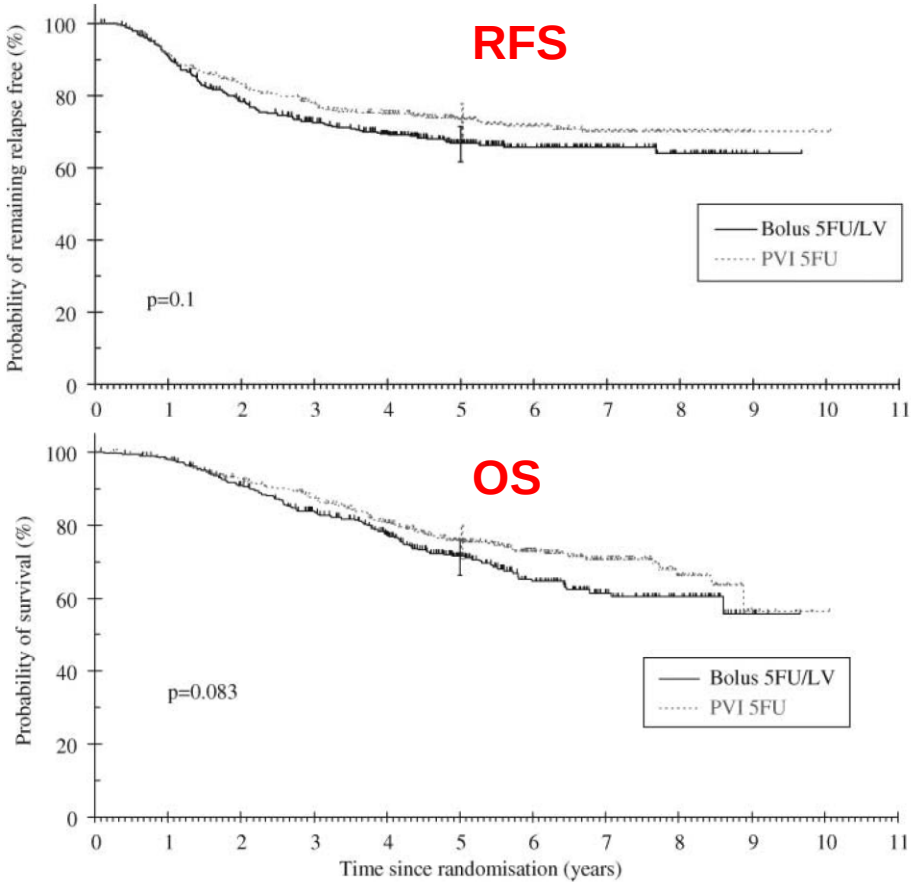
FOLFOX + 4%

(Cape ? + 3%)

FU/FA +15%

Total ~ 20%

12 weeks of CI 5-FU vs 6 months of 5-FU/LV



5 Year (%)	12 wks Ci 5-FU	6 months 5-FU/LV	HR (95% CI) p-value
RFS	73.3	66.7	0.8 (0.62-1.04) p=0.10
OS	75.7	71.5	0.79 (0.61-1.03) p=0.08

Likelihood of 12 wks of ci 5-FU being inferior: P<0.005

N=801

Chau et al., Ann Oncol 2005

IDEA (+*TBS) Recommendations

		Regimen	
		CAPOX	FOLFOX
Risk group	Low-risk (T1-3 N1) ~60%	3 months	(3-)6* months
	High-risk (T4 and/or N2) ~40%	3(-6*) months	6 months

* If choice for 6 months , then the last 3 months → Capecitabine alone

Thank you